

SEQUENCE LISTING

<110> Salonen, Jukka T.
 Marchesani, Marja
 Tuomainen, Tomi-Pekka
 Kaikkonen, Jari

<120> A DNA molecule encoding a variant paraoxonase, and uses thereof

<130> Ile102Val, also called Ile101Val variant

<140>

<141>

<160> 4

<170> PatentIn Ver. 2.1

<210> 1

<211> 1068

<212> DNA

<213> Homo Sapiens

<220>

<221> CDS

<222> (1)..(1068)

<223> Coding sequence for variant human paraoxonase (PON1) protein

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atg gcg aag ctg att	gcg ctc acc ctc ttg	ggg atg gga ctg gca ctc	48
Met Ala Lys Leu Ile	Ala Leu Thr Leu Leu	Gly Met Gly Leu Ala Leu	
1	5	10	15
ttc agg aac cac cag	tct tct tac caa	aca cga ctt aat gct ctc cga	96
Phe Arg Asn His Gln	Ser Ser Tyr Gln	Thr Arg Leu Asn Ala Leu Arg	
	20	25	30
gag gta caa ccc gta	gaa ctt cct aac	tgt aat tta gtt aaa gga atc	144
Glu Val Gln Pro Val	Glu Leu Pro Asn	Cys Asn Leu Val Lys Gly Ile	
	35	40	45
gaa act ggc tct gaa	gac atg gag ata	ctg cct aat gga ctg gct ttc	192
Glu Thr Gly Ser Glu	Asp Met Glu Ile	Leu Pro Asn Gly Leu Ala Phe	
	50	55	60
att agc tct gga tta	aag tat cct gga	ata aag agc ttc aac ccc aac	240
Ile Ser Ser Gly Leu	Lys Tyr Pro Gly	Ile Lys Ser Phe Asn Pro Asn	
	65	70	75
			80

agt cct gga aaa ata ctt ctg atg gac ctg aat gaa gaa gat cca aca	288
Ser Pro Gly Lys Ile Leu Leu Met Asp Leu Asn Glu Glu Asp Pro Thr	
85 90 95	
gtg ttg gaa ttg ggg gtc act gga agt aaa ttt gat gta tct tca ttt	336
Val Leu Glu Leu Gly Val Thr Gly Ser Lys Phe Asp Val Ser Ser Phe	
100 105 110	
aac cct cat ggg att agc aca ttc aca gat gaa gat aat gcc atg tac	384
Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr	
115 120 125	
ctc ctg gtg gtg aac cat cca gat gcc aag tcc aca gtg gag ttg ttt	432
Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe	
130 135 140	
aaa ttt caa gaa gaa gaa aaa tcg ctt ttg cat cta aaa acc atc aga	480
Lys Phe Gln Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg	
145 150 155 160	
cat aaa ctt ctg cct aat ttg aat gat att gtt gct gtg gga cct gag	528
His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu	
165 ^{Pro} 170 175 ^{Pro}	
cac ttt tat ggc aca aat gat cac tat ttt ctt gac ccc tac tta caa	576
His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln	
180 185 190	
tcc tgg gag atg tat ttg ggt tta gcg tgg tcg tat gtt gtc tac tat	624
Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr	
195 200 205	
agt cca agt gaa gtt cga gtg gtg gca gaa gga ttt gat ttt gct aat	672
Ser Pro Ser Glu Val Arg Val Val Ala Glu Gly Phe Asp Phe Ala Asn	
210 215 220	
gga atc aac att tca ccc gat ggc aag tat gtc tat ata gct gag ttg	720
Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu	
225 230 235 240	
ctg gct cat aag att cat gtg tat gaa aag cat gct aat tgg act tta	768
Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp Tyr Leu	
245 250 255 ^{Thr}	
act cca ttg aag tcc ctt gac ttt aat acc ctc gtg gat aac ata tct	816
Tyr Phe Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser	
260 265 ^{Thr} 270	
gtg gat cct gag aca gga gac ctt tgg gtt gga tgc cat ccc aat ggc	864
Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly	
275 280 285	
atg aaa atc ttc ttc tat gac tca gag aat cct cct gca tca gag gtg	912
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val	
290 295 300	
ctt cga atc cag aac att cta aca gaa gaa cct aaa gtg aca cag gtt	960
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val	
305 310 315 320	
tat gca gaa aat ggc aca gtg ttg caa ggc agt aca gtt gcc tct gtg	1008

Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val
 325 330 ^{Thr} 335
 tac aaa ggg aaa ctg ctg att ggc aca gtg ttt cac aaa gct ctt tac 1056
 Tyr Lys Gly Lys Leu Leu Ile Gly Tyr Val Phe His Lys Ala Leu Tyr
 340 345 ^{Thr} 350 1068
 tgt gag ctc taa
 Cys Glu Leu stop
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<210> 2
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 <212> PRT
 <213> Homo Sapiens

<400> 2

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 Phe Arg Asn His Gln Ser Ser Tyr Gln Thr Arg Leu Asn Ala Leu Arg
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 Glu Val Gln Pro Val Glu Leu Pro Asn Cys Asn Leu Val Lys Gly Ile
 35 40 45
 Glu Thr Gly Ser Glu Asp Met Glu Ile Leu Pro Asn Gly Leu Ala Phe
 50 55 60
 Ile Ser Ser Gly Leu Lys Tyr Pro Gly Ile Lys Ser Phe Asn Pro Asn
 65 70 75 80
 Ser Pro Gly Lys Ile Leu Leu Met Asp Leu Asn Glu Glu Asp Pro Thr
 85 90 95
 Val Leu Glu Leu Gly Val Thr Gly Ser Lys Phe Asp Val Ser Ser Phe
 100 105 110
 Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr
 115 120 125
 Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe
 130 135 140
 Lys Phe Gln Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg
 145 150 155 160
 His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu
 165 ^{Pro} 170 175 ^{Pro}
 His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln
 180 185 ^{Pro} 190
 Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr
 195 200 205
 Ser Pro Ser Glu Val Arg Val Val Ala Glu Gly Phe Asp Phe Ala Asn
 210 215 220
 Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu

[illegible]

$\langle 210 \rangle$ 3

<211> 1068

<212> DNA

<213> Homo Sapiens

<220>

<221> CDS

<222> (1)..(1068)

<223> Coding sequence for Human Paraoxonase (PON1) gene

$\langle 400 \rangle$ 3

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Met	Ala	Lys	Leu	Ile	Ala	Leu	Thr	Leu	Leu	Gly	Met	Gly	Leu	Ala	Leu	
1				5				10						15		
ttc	agg	aac	cac	cag	tct	tct	tac	caa	aca	cga	ctt	aat	gct	ctc	cga	96
Phe	Arg	Asn	His	Gln	Ser	Ser	Tyr	Gln	Thr	Arg	Leu	Asn	Ala	Leu	Arg	
			20					25					30			
gag	gta	caa	ccc	gta	gaa	ctt	cct	aac	tgt	aat	tta	gtt	aaa	gga	atc	144
Glu	Val	Gln	Pro	Val	Glu	Leu	Pro	Asn	Cys	Asn	Leu	Val	Lys	Gly	Ile	
		35					40					45				
gaa	act	ggc	tct	gaa	gac	atg	gag	ata	ctg	cct	aat	gga	ctg	gct	ttc	192
Glu	Thr	Gly	Ser	Glu	Asp	Met	Glu	Ile	Leu	Pro	Asn	Gly	Leu	Ala	Phe	
	50					55					60					
att	agc	tct	gga	tta	aag	tat	cct	gga	ata	aag	agc	ttc	aac	ccc	aac	240
Ile	Ser	Ser	Gly	Leu	Lys	Tyr	Pro	Gly	Ile	Lys	Ser	Phe	Asn	Pro	Asn	
65					70					75				80		
agt	cct	gga	aaa	ata	ctt	ctg	atg	gac	ctg	aat	gaa	gaa	gat	cca	aca	288
Ser	Pro	Gly	Lys	Ile	Leu	Leu	Met	Asp	Leu	Asn	Glu	Glu	Asp	Pro	Thr	
				85					90					95		

gtg ttg gaa ttg ggg atc act gga agt aaa ttt gat gta tct tca ttt	336
Val Leu Glu Leu Gly Ile Thr Gly Ser Lys Phe Asp Val Ser Ser Phe	
100 105 110	
aac cct cat ggg att agc aca ttc aca gat gaa gat aat gcc atg tac	384
Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr	
115 120 125	
ctc ctg gtg gtg aac cat cca gat gcc aag tcc aca gtg gag ttg ttt	432
Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe	
130 135 140	
aaa ttt caa gaa gaa gaa aaa tcg ctt ttg cat cta aaa acc atc aga	480
Lys Phe Gln Glu Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg	
145 150 155 160	
cat ⁴ aaa ³ ctt ¹⁴⁰ ctg ¹⁴⁵ cct ¹⁴⁵ aat ttg aat gat att gtt gct gtg gga cct gag	528
His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu	
165 ^{Pro} 170 175 ^{Pro}	
cac ttt tat ggc aca aat gat cac tat ttt ctt gac ccc tac tta caa	576
His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln	
180 185 190	
tcc tgg gag atg tat ttg ggt tta gcg tgg tcg tat gtt gtc tac tat	624
Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr	
195 200 205	
agt cca agt gaa gtt cga gtg gtg gca gaa gga ttt gat ttt gct aat	672
Ser Pro Ser Glu Val Arg Val Val Ala Glu Gly Phe Asp Phe Ala Asn	
210 215 220	
gga atc aac att tca ccc gat ggc aag tat gtc tat ata gct gag ttg	720
Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu	
225 230 235 240	
ctg gct cat aag att cat gtg tat gaa aag cat gct aat tgg act tta	768
Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp Tyr Leu	
245 250 255 ^{Thr}	
act cca ttg aag tcc ctt gac ttt aat acc ctc gtg gat aac ata tct	816
Tyr Phe Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser	
260 265 ^{Thr} 270	
gtg gat cct gag aca gga gac ctt tgg gtt gga tgc cat ccc aat ggc	864
Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly	
275 280 285	
atg aaa atc ttc ttc tat gac tca gag aat cct cct gca tca gag gtg	912
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val	
290 295 300	
ctt cga atc cag aac att cta aca gaa gaa cct aaa gtg aca cag gtt	960
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val	
305 310 315 320	
tat gca gaa aat ggc aca gtg ttg caa ggc agt aca gtt gcc tct gtg	1008
Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val	
325 330 335	
tac aaa ggg aaa ctg ctg att ggc aca gtg ttt cac aaa gct ctt tac	1056

1068

<210> 4
<211> 355
<212> PRT
<213> Homo Sapiens

<400> 4

Met	Ala	Lys	Leu	Ile	Ala	Leu	Thr	Leu	Gly	Met	Gly	Leu	Ala	Leu	
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			20					25					30		
Glu	Val	Gln	Pro	Val	Glu	Leu	Pro	Asn	Cys	Asn	Leu	Val	Lys	Gly	Ile
		35					40					45			
Glu	Thr	Gly	Ser	Glu	Asp	Met	Glu	Ile	Leu	Pro	Asn	Gly	Leu	Ala	Phe
	50					55					60				
Ile	Ser	Ser	Gly	Leu	Lys	Tyr	Pro	Gly	Ile	Lys	Ser	Phe	Asn	Pro	Asn
65					70					75					80
Ser	Pro	Gly	Lys	Ile	Leu	Leu	Met	Asp	Leu	Asn	Glu	Glu	Asp	Pro	Thr
				85					90					95	
Val	Leu	Glu	Leu	Gly	Ile	Thr	Gly	Ser	Lys	Phe	Asp	Val	Ser	Ser	Phe
			100					105						110	
Asn	Pro	His	Gly	Ile	Ser	Thr	Phe	Thr	Asp	Glu	Asp	Asn	Ala	Met	Tyr
		115					120					125			
Leu	Leu	Val	Val	Asn	His	Pro	Asp	Ala	Lys	Ser	Thr	Val	Glu	Leu	Phe
	130					135					140				
Lys	Phe	Gln	Glu	Glu	Glu	Lys	Ser	Leu	Leu	His	Leu	Lys	Thr	Ile	Arg
145					150					155					160
His	Lys	Leu	Leu	Phe	Asn	Leu	Asn	Asp	Ile	Val	Ala	Val	Gly	Phe	Glu
				165 ^{Pro}					170					175 ^{Pro}	
His	Phe	Tyr	Gly	Thr	Asn	Asp	His	Tyr	Phe	Leu	Asp	Phe	Tyr	Leu	Gln
			180					185				190 ^{Pro}			
Ser	Trp	Glu	Met	Tyr	Leu	Gly	Leu	Ala	Trp	Ser	Tyr	Val	Val	Tyr	Tyr
	195					200						205			
Ser	Pro	Ser	Glu	Val	Arg	Val	Val	Ala	Glu	Gly	Phe	Asp	Phe	Ala	Asn
	210					215					220				
Gly	Ile	Asn	Ile	Ser	Pro	Asp	Gly	Lys	Tyr	Val	Tyr	Ile	Ala	Glu	Leu
225					230					235					240
Leu	Ala	His	Lys	Ile	His	Val	Tyr	Glu	Lys	His	Ala	Asn	Trp	Tyr	Leu
				245					250					255 ^{Thr}	
Tyr	Phe	Leu	Lys	Ser	Leu	Asp	Phe	Asn	Tyr	Leu	Val	Asp	Asn	Ile	Ser
	260							265					270		
Val	Asp	Pro	Glu	Tyr	Gly	Asp	Leu	Trp	Val	Gly	Cys	His	Pro	Asn	Gly

	275					280					285								
Met	Lys	Ile	Phe	Phe	Tyr	Asp	Ser	Glu	Asn	Pro	Pro	Ala	Ser	Glu	Val				
	290					295					300								
Leu	Arg	Ile	Gln	Asn	Ile	Leu	Thr	Glu	Glu	Pro	Lys	Val	Thr	Gln	Val				
305					310					315					320				
Tyr	Ala	Glu	Asn	Gly	Thr	Val	Leu	Gln	Gly	Ser	Tyr	Val	Ala	Ser	Val				
			325						330	Thr				335					
Tyr	Lys	Gly	Lys	Leu	Leu	Ile	Gly	Tyr	Val	Phe	His	Lys	Ala	Leu	Tyr				
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Cys	Glu	Leu	stop																

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<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer pair

<400> 5

gtgcacctagcacctgcttg

<210> 6

<211> 21

<212> DNA

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<223> Description of Artificial Sequence: PCR primer pair

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cagttggaaggagcaaaatgg

<210> 7

<211> 20

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<223> Description of Artificial Sequence: PCR primer pair

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<210> 8
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<210> 18
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<210> 21

<211> 20

<212> DNA

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<223> Description of Artificial Sequence: PCR primer pair

<400> 20

ctgaacaagacatggcaaggc